COMMENTS ON THE ECOFRAM AQUATIC DRAFT REPORT

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The following pages contain a review of the Ecological Committee on FIFRA Risk Assessment Methods (ECOFRAM) Aquatic Draft Report. The reviewer examined the entire report, but particularly focused on the exposure assessment. The following pages contain:

I. Peer input comments on the ECOFRAM Aquatic Draft Report
II. Answers to the questions posed in the Charge to ECOFRAM Peer Input Panel Members
III. Suggestions for improving toxicity tests for the purposes of probabilistic assessment

I. PEER INPUT COMMENTS

ECOFRAM Aquatic Draft Report strengths

The ECOFRAM draft report provides a basic framework for how to approach probabilistic risk assessment. The report addresses issues such as site, species, and temporal difference issues in exposure and effects. This approach required viewing current data requirements and methodologies in a new light, with an eye towards how best to adopt the current deterministic framework to a new paradigm. The panel's work yielded a good approach to combining exposure with effects probabilities, especially given limited resources and time.

The chapter on exposure assessments provided a number of extremely useful recommendations, including suggestions for improving the exposure-relevant FIFRA Part 158 guideline tests. The workgroup's recommendations are worth noting here because of their importance in improving exposure assessments. The recommended changes included: obtaining rate constants for degradate formation and decline; obtaining hydrolysis rate constants as a function of temperature; determining quantum yields; using multiple soils for soil aerobic metabolism studies; enhancing batch equilibrium study design and analysis; modifying aquatic metabolism studies to separate degradation in the water column and sediment; conducting foliar dissipation and washoff studies for foliar pesticides; focusing anaerobic soil metabolism studies on degradation in subsoil horizons and aquifers; and conducting studies of potential of uptake from soil into plants. A number of useful suggestions were made with relation to data submission and model input documentation in risk assessment reports. ECOFRAM also recommended the update of the EPA one-liner database, a database of pesticide chemical properties, as soon as possible. The report also suggests the submission of product data, by registrants, to the ARS Pesticide Properties Database. ECOFRAM made the very useful suggestion that a FIFRA risk assessment web page should be set up to provide access to approved models, databases, GIS coverages and associated meta-data, to help standardize risk assessment approaches. The report also provided descriptions of the current exposure models, including their assumptions and limitations, and listed a number of major improvements to be made in future model versions. The suggestion was made that the EPA clarify guidance on accepted methods for calculating input parameters such as

degradation rate. ECOFRAM made the recommendation that a new suite of modeling tools should be developed with well-documented coding and the capability of adding modules as improved approaches and algorithms are developed, with the objective of approaching the goal of accounting for mass balance. The report made the important point that any new model development should be guaranteed of support and adequate manpower to perform improvements and longer term development.

Several issues that were insufficiently addressed or are believed to need improvement are listed below.

ECOFRAM document: Areas that Need Improvement
Major points for consideration are outlined in the following pages.

Aquatic Exposure-Specific Comments

1. Overall, the validity and conservatism of the exposure models, as they are currently used, were assumed to be sufficient to proceed with probabilistic assessment. The ECOFRAM exposure workgroup did make some useful specific suggestions to improve model validation (noted below), but, in general, appeared to operate under the assumption that the exposure models, as they are currently used, are both already well-validated and conservative. The ECOFRAM panel noted, and the SAP repeatedly emphasized, the importance of validating estimated concentrations and estimated effects with "real world" data. However, the workgroup minimized the use of field research to assess new approaches, such as the joint probability curves, or to validate estimated environmental concentrations of new chemicals. ECOFRAM is relying heavily upon the FIFRA Environmental Model Validation Task Force project, and appears to expect that the validation project will indicate that the current Pesticide Root Zone Model (PRZM) model is valid as is. This may be warranted, but is worth noting. ECOFRAM recommended that a group should assess the need for a more detailed validation of Exposure Analysis Modeling System (EXAMS). It is also worth noting that the entire aquatic probabilistic assessment is based on the assumption that EXAMS is also valid.

   The report provided a useful outline of some additional data needed to support model development and validation including: a clearer understanding of spatial variability associated with soil degradation at the micro and macro spatial scales; descriptions of effects of water content, aeration, and microbial activity in a way that can be routinely parameterized for modeling; compilation of literature on the extent of oxygen and organic carbon transport to subsoils and the effect on subsoil degradation; information on the relative importance of and methods to quantify volatilization from leaf surfaces; data on variations of concentrations within a water body; a better accounting within models of the occurrence of multiple soils within a watershed/field; the preparation of comprehensive regional water database with respect to volume, depth, drainage area, and slope; and data on the effects of mitigation to help validate mitigation impact modeling. The reviewer notes that an additional exposure

model validation issue that needs to be addressed includes the evaluation of the effects of preferential flow.

2. The use of distributions of model input parameters was not adequately addressed; the document appears to suggest, at least in the near term, the continued use of single value input parameters. The use of input parameter distributions would provide useful information on within site variability in exposure. ECOFRAM did suggest that the EPA should provide clear guidance how best to express variation around the single input value selected for model inputs. However, it may have been more useful for the workgroup to attempt to address this issue directly. Variability and uncertainty in input parameters are important aspects of exposure probability estimation.

3. The expansion of the exposure analyses to larger scales at higher tiers is recommended as a refinement. This may result in potential scale bias. The approach described by the exposure workgroup may have the result of essentially diluting the exposure and effects of smaller scale, ecologically sensitive areas identified in tier 1, by moving towards national or regional scale analyses, which would include more low impact areas. This approach does not diminish the exposure and effects in the original, smaller scale, ecologically sensitive areas.

   Additionally, since the some of the factors which would affect variability in exposure were not fully examined and quantified at the smaller scale (metabolism, etc.), the uncertainty within a given site remains the same as the current level, and has now been propagated to a multiple sites and a larger scale, increasing the overall uncertainty. Therefore, this approach leads to an apparent decrease in effect through dilution of exposure estimates, while propagating variability that has not been fully evaluated.

   The exposure workgroup made the recommendation that refined runs should be reported alongside data prepared using standard assumptions. This could be applied to the use of basin scale models. The field scale results should be reported simultaneously.

4. Related to the above point, the use of more variables at the higher tiers (e.g. landscape parameters) in the risk assessment may lead to increased uncertainty, particularly if variability in additional inputs is not well understood

5. Monitoring studies and field testing have been minimized. The ECOFRAM report states that monitoring results “should not be given undue emphasis.” Since well-designed, specific monitoring studies and dedicated field experiments are the only way to verify actual environmental concentrations, their importance and use should not be minimized.

   The exposure workgroup recommends the use of ongoing monitoring programs, such as NAWQA, to evaluate model estimates, in lieu of a registrant conducting a monitoring study or field testing for its specific product. It should be noted that ongoing studies of large numbers

of chemicals must be used judiciously, when comparing them to model output. Specific programs may not be geared specifically toward ecologically-important habitats; thus many of the sample sites are not likely to reflect ecologically-significant aquatic habitats in the upper watersheds. Some monitoring programs have, in the past, involved the measurement of parent compounds only, for many of the chemicals studied; degradates or metabolites were not measured in many cases. Furthermore, for many of the monitoring projects, the relationship between sample collection time and application may not be known. Therefore, peak exposure levels may frequently be missed in ongoing studies using periodic sampling. These general monitoring studies may provide extremely useful information, but their specificity and limitations must be understood when using the data for registration purposes.

Field studies involving a known application method and timing, with the optimized analysis of parent compound and relevant degradates, will provide the most useful site-specific data to verify model output.

6. The aquatic report repeatedly states that the Tier 1 and 2 exposure models, as currently used, are "highly conservative." Empirical evidence must be provided to validate this assumption. According to EFED personnel, occasionally environmental levels actually exceed GENeric Estimated Environmental Concentration (GENEEC) (Tier1) or PRZM/EXAMS (Tier 2) values.

7. The exposure workgroup assumed:
   a.) "Water concentrations are homogenous within the range of the organism being considered."
   b.) "The dominant route of exposure for an aquatic organism is via the water, dietary and behavioral factors can be ignored under all but the most complex analyses." Dietary and sediment exposures have been excluded and minimized, repsectively. This may lead to under predicting exposure and effect.

8. The issue of degradate modeling and/or monitoring was not addressed in the report, as noted on page 3-12. An approach or recommendation for the inclusion of degradates in the probabilistic risk assessment would have been very useful, and may be, in many cases, critical to an accurate assessment of risk.

9. The effect of groundwater transport of pesticides into surface water bodies, or into irrigation water sources, was not considered.

10. A tool noted as developed to help standardize half-life calculations was described as provided (p. 3-86), but was not found, and so could not be evaluated.

11. The report states that "tier 4 approaches reality even more closely because typically it will bring into play all the fields of the crop of interest that are UNEXPOSED (report's

capitalization) as well as the other areas of the watershed which are not even the crop of interest." (p. 3-105). It is important to recognize, while refining the assessment, that this approach will not account for usage of the same pesticide on other crops, nor the effects of other pesticides applied within the same area.

Aquatic Effects-Specific Comments

1. No additional data requirements were recommended for risk assessments at Tier 2, over that required at Tier 1. The aquatic effects section particularly stipulates no new data requirements for Tier 2; Tier 2 effects analysis will simply involve the reevaluation of the Tier 1 deterministic data set. (The whole dose-response curve will be used at Tier 2, instead of just the Tier 1 LC_{50}.) The ECOFRAM aquatic workgroup notes that "the purpose of higher tiers is to reduce uncertainty in the risk characterization and/or, by generating additional data, to replace the conservative assumptions with increasingly representative values." With no new data requirements for Tier 2, there appears to be little reduction in effects uncertainty, relative to Tier 1. It may be possible to combine the Tier 2 effects approach with the Tier 1 exposure approach, to yield information on the probability of effect in generic vulnerable areas.

2. The Tier 2 probabilistic effects framework is not probabilistic with respect to several important aspects:
   a.) The framework does not address species sensitivity differences until Tier 3, and therefore cannot be said to be probabilistic with respect to species differences within a taxa at the Tier 2 probabilistic level.
   b.) Within species variations in sensitivity with life-stage is should be more fully addressed.
   c.) The framework does not appear address variations in effects with different formulations.

   ECOFRAM did, however, recommend including the Daphnia life-cycle test, and fish early-life stage tests to Tier 1, which is an improvement over the current paradigm.

3. ECOFRAM does not consider effects on aquatic vertebrate reproduction until Tier 3. Therefore, the probability of this effect cannot be assessed at lower tiers. A fish full life- cycle, or, at a minimum, an abbreviated fish reproduction test, should be considered for inclusion Tier 1, in order to assess the potential for endocrine or reproductive disruption.

4. The sediment toxicity section in chapter 4 (4-106 to 4-111) could be more fully integrated into the rest of the document and risk assessment picture, and sediment toxicity could be more fully addressed at an early tier. If chemical parameters suggest partitioning of a chemical into sediment, toxicity should be addressed at Tier 1, with at least one benthic species. The ECOFRAM report states that Tier 1, long-term objectives should include determining the potential need to consider sediment toxicity impacts, but notes that this is currently not possible in Tier 1. The workgroup recommended including this functionality in the next

generation of exposure models, but later noted that the generation of a new Tier 1 model is not a high priority. The Tier 1 approach should include an assessment of the need for sediment toxicity tests now, based on chemical characteristics.

Based on the description chapter 2 of the report, during the interim period prior to the creation of the next generation of models, the ECOFRAM workgroup does not recommend considering sediment toxicity until Tier 3. In Tier 3, the workgroup also only recommends comparing the PRZM/EXAMS output for pore water concentrations to acute and chronic invertebrate toxicity tests results, prior to undertaking an acute or chronic sediment toxicity test with a benthic species (p. 2-34). The Tier 3 approach described in chapter 2 involves two extrapolations of uncertain validity: an extrapolation of model output to actual field sediment and pore water concentrations, and an extrapolation from effects of such concentrations, in water, on planktonic or pelagic species to the effects of the same concentration, in sediment, on benthic species. Both of these extrapolations involve undescribed or unknown errors, and will yield highly uncertain results. The report notes this uncertainty as well, and thus it would seem prudent to recommend direct testing on a benthic species at a lower tier, if the chemical properties suggest potential exposure.

In the effects chapter (ch. 4), the approach to sediment toxicity testing is described somewhat differently. Toxicity testing, based on OPPTS guidelines that are not yet finalized, is expected to be triggered if *any* of the following conditions are met: the chemical parameters (K_{oc}, etc) indicate partitioning to sediment will occur, the pesticide is persistent in sediment (half-life $\geq$10 days), or the modeling output indicates potential toxicity relative to planktonic/pelagic test species data. Chapter 2 of the report does not discuss consideration of testing solely based on partitioning or half-life in sediment; testing is only triggered after extrapolation to a non-benthic species indicates potential toxicity.

Recent declines in benthic species in the Chesapeake Bay (e.g. oyster, crabs) indicate the relevance of estimating effects on these species. Furthermore, many benthic organisms are commercially important species consumed by humans (flatfish, clams, oysters, crabs, catfish, etc). Their importance in an ecosystem and their significance as potential sources of pesticides to humans via diet should not be overlooked.

4. Additional consideration should be given to semi-aquatic species. Amphibians, reptiles, and other groups (e.g. ducks, geese, piscivorus birds, aquatic mammals, insects) that may be exposed to pesticides in both aquatic and terrestrial habitats are not well-addressed in the document, nor are they in current risk assessment methods. “Effects on reptiles and amphibians” was noted as an information gap by ECOFRAM. A more complete discussion of how to approach the quantification of both aquatic and terrestrial exposures for amphibians would be extremely useful, in lieu stating that there is a great deal of uncertainty. The apparent separation of the aquatic and terrestrial workgroup approaches appears to have led to an incomplete risk assessment picture. This is particularly of concern, since amphibians

appear to be undergoing a worldwide population decline. Risk assessment for these species may therefore be especially critical.

Furthermore, there was a somewhat misleading reference to previously completed toxicity testing with amphibians. The ECOFRAM workgroup noted that Mayer and Ellersieck (1986) published a report on inter-taxon evaluations of aquatic toxicity. ECOFRAM stated that the report included 66 species and 410 chemicals. The workgroup noted that two species of amphibians were included, and the chemicals tested were uniformly less toxic to these two amphibians than to the standard freshwater test organisms. Based on this information, ECOFRAM concluded that the standard test organisms could serve as surrogates for amphibians. This may be an overstatement, since only 20 chemicals were actually tested on the toad, and only 13 on the single frog species tested, not the 410 chemicals mentioned. Furthermore, nearly half of the chemicals tested on amphibians are no longer registered. Mayer and Ellersieck (1986) themselves noted that in other studies (Birge *et al.*, 1980; Black *et al.*, 1982), when other common species were tested (leopard frog, *Rana pipiens* and European common frog, *R. temporaria*), amphibians were found to be as sensitive as salmonids, the most sensitive fish family. Therefore, the comparison of amphibians to aquatic test species is rather limited in its scope as well as its current relevance, and data indicates that some amphibians are not less sensitive than fish. The case for amphibian toxicity being covered by surrogate species should not be overstated. Additional toxicity testing with amphibians and reptiles appears to be warranted, unless additional studies that indicate relative insensitivity of amphibians are outlined.

5. The SAP recommended using biomarkers in risk assessments; the ECOFRAM aquatic report did not fully explore the use of biomarkers or indicators of sublethal effects. Measurement of indicators of sublethal effects would be extremely useful tools in evaluating the probability of subtle effects occurring that may impact on the physiological status of an animal. These effects may not be grossly observable, but may have a pronounced effect on an organism (e.g. immunosuppression). For example, exposure of oysters to sublethal doses of organic chemicals has been demonstrated to enhance preexisting parasitic infection (*Perkinsus marinus),* and was shown to increase susceptibility to experimentally induced infection in a dose-dependent manner (Chu and Hale, 1994). Furthermore, biomarkers may be useful indicators of future viability and reproductive fitness. Toxicity tests used in pesticide regulation should be improved to reflect current scientific knowledge and practices. It would be useful if the significance of biomarkers, including a review of the literature, was somewhat further explored in the final report.

6. The SAP also recommended expanding the scope of data requirements to include additional toxicity tests with additional species, life-stages, and formulations. The ECOFRAM report did not fully address formulations in effects assessments, and did not recommend additional toxicity tests with additional species for the first two tiers, other than including two current chronic tests in Tier 1. The SAP also recommended reinstating field studies, ECOFRAM did

not pursue this.

7. The effects workgroup stated that " most of these tools for higher tier aquatic effects analysis (e.g time varying exposure tests, species sensitivity, population analysis) are not probabilistic, and do not address stochastic uncertainty as do many of the techniques for refined exposure analysis." However, they noted that they these tools do reduce uncertainty for these particular relationships.

Integrated Exposure/Effects Comments

1. There appears to be no recommended cutoff at any tier that would remove a chemical from consideration for further refinement and higher tiers, due to an unacceptably large exceedence of levels of concern. This presents the problem of continual refinement, and expenditures of time and resources, for a chemical which is likely to be unacceptably toxic in the environment, based on lower tiers. This is a concern not only for the registrant, but for the EPA, given the limited nature of resources for registration activities. Cutoff criteria will need to be established at some point, in the joint process of developing a probabilistic framework, to prevent the occurrence of endless refinement.

2. The heart of the probabilistic approach recommended by the aquatic workgroup is the use of joint probability curves. This approach of comparing model data directly to experiment results may involve inherently different errors. For example, it may be the case that the confidence intervals around the model output are so large that mortality cannot be known with any certainty, yielding, in extreme cases, the result of expected environmental concentrations having a probability of a very wide range of mortality. The variability and uncertainty about the estimates of exposure and effects were not described in the report. Omitting the error bars for each axis leads to an unrealistic expectation of the narrowness and exactness of the probabilistic conclusion.

   The use of joint probability based on regional or national scale exposure assessments also may mask the fact that some ecologically sensitive areas could have extremely poor effects outcomes, by essentially averaging exposure results from impacted areas with low impact areas, as was mentioned in the exposure comments. The averaging process does not reduce the effect on high impact areas, and in fact may lead risk managers to a misunderstanding of the nature of the effects distribution. When joint probability curves are used, they should be created for single-site vulnerable areas, in addition to regional or national scale areas, so that the effects of scale can be evaluated and compared more easily.

   The joint probability curve concept should be validated with field data before use, and the errors in the exposure and effects terms should be fully addressed. ECOFRAM noted the SAP panel's issues: "There is a great need to better understand the functional relationship between the tools used to estimate effects, and exposure estimates, and actual effects under field

conditions. These relationships would most likely be the foundation for any model, deterministic or probabilistic. In the absence of this research, which the Panel (SAP) suggested is long overdue, the questions associated with the present methodologies will persist even if more sophisticated methodologies are developed" ECOFRAM p.2-5.

General Comments

1. The charge given to ECOFRAM encouraged delaying an analysis of indirect effects, due to time constraints. However, it is worth noting that ignoring indirect effects may lead to a large underestimation of the probability of effects. For example, loss of aquatic invertebrate species, even for relatively short durations, as a result of chemical exposure, may have a profound effect on survival of juvenile fish relying on the affected invertebrate species as a food source. Major indirect effects should be brought into the risk assessment process as soon as possible.

2. The importance of biodiversity was minimized through the underlying assumption that "some population reduction are of no ecological significance, " and that "effects on an individual population are not necessarily of concern as long as the function the population performs can be overtaken by other species."

3. The final document should contain a more complete evaluation of current literature, other than the authors' own. Several issues appear to be presented without a full evaluation of all peer-reviewed literature. The document contains a number of scientific conclusions, some potentially controversial, without any references.

4. Chapter 2 states that "assuming clear generic guidance on the tier system is defined, it is likely that much of the work encompassed by Tier1 to 3 can be conducted by the registrant prior to discussion with OPP EFED." EPA input prior to completing the work up to Tier 3 is highly advisable.

5. The report states that "risk assessors must be willing to evaluate the relative merits of risk mitigation even in the absence of data," and " the risk reduction/mitigation process can begin at any time during the process of reviewing a pesticide."A lack of data to evaluate the effects of mitigation options should be temporary situation, hopefully. Additional research on the effects of mitigation options should be conducted to inform decisions.

6. Basic editorial/stylistic comments:
   a.) Chapter 3 (exposure) in particular, as well as parts of chapter 2, need to be thoroughly edited. Chapter 3 is quite repetitious, with a great deal of apparent cut and pasting through sections.
   b.) Some references cited in the body of the text in the exposure chapter are missing from the appendix (e.g. Dyson *et al.*, 1998; Esterley, 1998)
   c.) A figure representing a typical exposure distribution generated by current models was

omitted (Fig. 3-10), even though this format for expression of exposure was noted as "fundamental to the approach recommended by ECOFRAM." The final report should include this figure.

d.) The tables listing the input parameters for GENEEC and PRZM/EXAMS should be updated to reflect current guidance. For example, the multiplication factor to be applied when only a single soil aerobic metabolism half-life is available for PRZM/EXAMS input was listed as 2.3 (p. 3-113). Current guidance states that the factor should be 3.

II. RESPONSE TO PEER INPUT QUESTIONS:

1. Is the draft scientifically sound?

The underlying basis of the draft is scientifically sound, however the data requirements proposed to create probabilistic risk assessments are insufficient at the lower tiers to make scientifically sound judgements of effect levels.

Suggestions on how to improve the scientific defensibility of the report.

a.) Full field validation of models prior to their use in probabilistic assessment should be recommended.
b.) The workgroup should conduct a few comparative case study analyses of the effects of scale on probabilistic outcome.
c.) An approach to the use of distributions of model input parameters should be included now, and sensitivity analyses should be recommended for model inputs for each chemical and use.
d.) Additional taxa and life-stages should be included in tier 2 testing to come to a more complete understanding of the probability of effects.
e.) Additional replicates should be considered for basic tests, with a minimum replicate number per dose set at four.
f.) A fish full life cycle, or, at a minimum, an abbreviated fish reproduction test should be recommended at Tier 1, in order to assess the potential for endocrine or reproductive disruption.
g.) An additional test for chronic aquatic invertebrate toxicity using a sexually reproducing freshwater species should be considered. *Daphnia* are primarily parthenogenetic.
h.) The report should include a more complete discussion of formulated product testing to evaluate the effects of multiple active ingredients or inerts.
i.) Sediment toxicity testing with benthic species should be included at Tier 1 if chemical characteristics indicate partitioning from the water to sediment.
j.) An exceedence cutoff should be discussed to limit the resources spent on unacceptably toxic compounds.
k.) An approach to validating the joint probability curve concept should be outlined, and the variability in the exposure and effects terms should be fully addressed.
l.) The effect of groundwater transport of pesticides into surface water bodies should be addressed.
m.) A more complete literature search on the effects of species loss on ecosystem status would be useful.

2. Did the ECOFRAM workgroup address the charge to ECOFRAM as described in the background document?

There were several aspects to the charge to ECOFRAM. The major points will be addressed individually to clarify explanation.

a.) The primary charge to ECOFRAM was to develop a process and tools for predicting the magnitude and probabilities of adverse effects, focusing on direct acute and chronic effects to individuals and populations of high risk species.

The aquatic workgroup developed a good process and outlined several tools to conduct probabilistic risk assessments, focusing on the assigned groups. The primary strength of the document was the creation of a framework for how to approach probabilistic risk assessment, and the group's discussion of and approach to joint exposure and effects probabilities. The exposure tools developed primarily involved a refinement or elaboration upon currently used models. The Risk Assessment tool to evaluate Duration and Recovery (RADAR), for examining temporal variation in exposure, is a useful and needed tool. The Multiple Scenario Risk Assessment Tool (MUSCRAT), which originated outside the scope of ECOFRAM, may also be a useful tool. These tools, however, must be judiciously used, with care given to not obscuring and ignoring actual negative field scale effects on sensitive ecosystems, through apparent reduction in risk by moving to a large scale assessment.

b.) Tools developed were to have a reasonable scientific certainty or be able to be validated within a reasonable time frame.

The tools developed do not currently have scientific certainty. Complete validation of the current exposure models used, GENEEC, PRZM3 and EXAMS, has not been fully described. Therefore, tools primarily derived from these models (RADAR, MUSCRAT) are also not currently fully validated via field data. If a concerted effort was made by the Agency and stakeholders, the exposure tools should be able to be fully validated within a reasonable time frame. Due to the great reliance of the framework outlined in the ECOFRAM report on exposure modeling in lieu of actual field measurements, the completion of validation is essential for probabilistic risk assessment. Furthermore, because of the use of single value input parameters used in the models, each site's exposure variability is driven by variations in weather and soil characteristics at that site; within site variations in exposure due to variability in parameters such as soil metabolism and sorption are not considered.

Additional tools outlined in the report include the use of joint probability curves, which compare the probability of exposure exceedence with the probability of mortality. The variability and uncertainty about the estimates of exposure and effects need to be addressed. Ignoring the confidence intervals for each joint probability curve axis leads to an unrealistic expectation of the narrowness and exactness of the probabilistic conclusion.

c.) Methods developed were to consider species sensitivity, environmental fate variables, routes of exposure, product formulation, application techniques, habitat types, etc.

Species sensitivity issues were considered only at tier 3; species sensitivity should be moved to a

lower tier. The routes of exposure issue was not fully addressed for aquatic ecosystems, since dietary exposures were not considered and sediment exposures were not addressed until the higher tiers. Biological effect of product formulation did not appear to be fully considered; examination of formulation impacts on environmental fate were mentioned only as potential Tier 3 fate-o-cosm or small-scale runoff refinements. Application techniques and habitat types were addressed through model inputs. A number of population models were described for higher tier evaluations, as was time-to-event analysis, and well as other effects models.

d.) The ECOFRAM workgroup was also tasked with defining additional development or validation efforts needed for probabilistic assessment.

A number of research needs and validation efforts needed were described, but validation of the joint probability curve approach was not fully addressed, and the general validation of current exposure models appeared to be assumed.

It is worth noting that the ECOFRAM workgroup did address most of the points described in their charge, however, several of the issues previously described by the SAP, which are relevant to probabilistic risk assessment, were not fully addressed. Time constraints appeared to rule out fuller consideration, but the issues are worth noting here. These issues include: estimating exposure and effects based on active ingredients, without considering formulations and degradates; amphibian and reptile exposures and effects; a full evaluation of the use of biomarkers as endpoints; the issue of variability in effects based on life-stage; a discussion of the wide range and use of extrapolations and their validity; and a more detailed analysis of validation of current exposure models through field studies.

3. What are the limitations for predicting risk using the ECOFRAM approach?

Limitations include the lack of sufficient effects data requirements at Tier 2 to make a truly probabilistic assessment. Additional species and life-stage tests would be necessary to more fully estimate the probability of effects. The approach is also limited by an incomplete description of the confidence intervals around risk estimates based on joint probability curve analyses. Furthermore, the use of the basin scale approach may obscure the risk to ecologically sensitive areas through essentially averaging over a larger area.

A few important issues for predicting risk were not fully addressed: the effects of formulation on toxicity, since only active ingredients are generally tested; calculations of exposure levels for pesticides that are used on multiple crops within a limited area, since generally only the risk posed by usage of a pesticide on single crops is evaluated; and perhaps most importantly, the biological effects of multiple chemical exposures. The last two issues may contribute to a significant underestimation of risk.

4. What areas of the report need to be strengthened?

See answer to question 2 above.

5. What is the minimum level of technical information/scientific understanding necessary to evaluate whether risk mitigation would be necessary and/or effective?

Risk management options can be considered when the uncertainty and variability in the risk assessment data is understood. In order to accomplish this, the Tier 3 effects assessment tools, including species sensitivities distributions, fish full life-cycle chronic toxicity or abbreviated fish reproductive tests, and, in the case of lipophilic chemicals, sediment toxicity tests, could be coupled to the Tier 2 exposure analysis. Mitigation could then be approached with a fuller understanding of potential effects and the efficacy of mitigation. However, the additional issues of multiple crops, formulations and chemicals, listed in question 3, will still not be addressed. The results (effectiveness in the real world) of the mitigation options also need to be understood.

III. SUGGESTIONS FOR IMPROVING TOXICITY TESTS FOR PROBABILISTIC RISK ASSESSMENTS

1. Increase Statistical Supportability of All Toxicity Tests
Proposed change: Addition of replicates for toxicity tests, setting a minimum replicate number of four per dose.
Purpose: The suggested minimum replicate number for acute tests should be increased to four to provide a minimum sample size reasonable for statistical analyses. Currently only two replicate tanks are frequently used for some acute toxicity tests (e.g. fish). A minimum replicate number of four would still yield a reasonable number of data points in the case of total loss/failure with one of the replicates tanks.

2. Improve Certainty of Extrapolation to Untested Aquatic Species.
Proposed change: Addition of acute toxicity protocols for additional aquatic species (e.g. freshwater gastropod or bivalve, and insect larvae test)
Purpose: Additional species should be tested to provide more representative toxicity data over taxa.

3. Improve Certainty of Sediment Toxicity Risk Estimates
Proposed change: Addition of sediment toxicity testing with a benthic species at an early tier, with dosed sediment. If the use pattern of the chemical indicates the possibility of estuarine/marine exposure, an estuarine/marine benthic species should also be tested.
Purpose: To reduce the current uncertainty in testing regarding the toxicity of pesticides to benthic organisms.
When Recommended: For all hydrophobic chemicals with outdoor uses

4. Improve Certainty of Risk Assessments for Amphibian Species
Proposed change: Add amphibian toxicity test to guideline studies.
Purpose: Current testing does not sufficiently address species that may be exposed to pesticides in both aquatic and terrestrial habitats. This is particularly of concern, since amphibians appear to be undergoing a worldwide population decline. Risk assessment for these species may therefore be especially critical.

5. Improve Certainty of Chronic Risk Assessments for Wider Range of Aquatic Invertebrate Species
Proposed change: Add chronic invertebrate toxicity test with sexually reproducing species to guideline studies.
Purpose: Current aquatic invertebrate chronic toxicity testing involves the use of a primarily parthenogenetic species, *Daphnia magna*. This testing does not fully address the potential effects of a pesticide on sexually reproducing species, and therefore does not fully address the effects of potential endocrine disruption.

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